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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/058,456	01/28/2002	Pascale Pouzet	1/1168	4239

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EXAMINER

ANDERSON, REBECCA L

ART UNIT PAPER NUMBER

1626

DATE MAILED: 08/26/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/058,456

Applicant(s)

POUZET ET AL.

Examiner

Rebecca L Anderson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-30 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.

- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Claims 1-30 are currently pending in the application.

Claim Objections

Claim(s) 9-10, 19-20, and 29-30 are objected to for being substantial duplicates of claims 1, 11, and 21 respectively. When two claims in an application are duplicates, or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to reject the other as being a substantial duplicate of the allowed claim. M.P.E.P. 706.03(k). Claims 9-10, 19-20 and 29-30 are substantial duplicates of claims 1, 11 and 21 because the terms "iminoimidazolidine" in claim 9 and "aminoimidazoline" in claim 10 are just ways of describing the compounds as instantly claimed in claim 1 by word descriptions instead of the structural depictions of formulas I and II as seen in claim 1, and therefore the claims are all still claiming the same inventions. This rejection can be overcome by deleting the duplicate claims 9-10, 19-20, and 29-30.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of urinary incontinence does not reasonably provide enablement for bladder diseases. The specification does not enable

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any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In In re Wands, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case, applicants are claiming a method of treating "urinary incontinence" or "a bladder disease". However, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. As defined the claims read on treating all bladder diseases, however, the only bladder disease mentioned in the specification is urinary incontinence. The term bladder disease includes a host of various diseases such as bladder cancer, interstitial cystitis, urinary tract infections, and pediatric reflux, which is broader than the enabling

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disclosure. The various types of bladder diseases have different causative agents, involve different cellular mechanisms, and, consequently, differ in treatment protocol. Therefore, based on the unpredictable nature of the invention and the state of the prior art, the extreme breadth of the claims, and the fact that the specification is short of any pharmacological data (animal models, in vitro or in vivo testing) in regards to the treatment bladder diseases except for urinary incontinence, one skilled in the art could not use the claimed invention without undue experimentation. This rejection can be overcome by deleting "or a bladder disease" from claims 21-30.

Claims 7 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The numbers in brackets after each compound named appear to be relating the compounds back to compounds in the specification. However, these bracketed numbers are vague and confusing and therefore should be eliminated from the claim language.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

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1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

Claims 1-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/32939 and DE 3712385. The English equivalent of WO 96/32939 is the national stage entry of PCT/EP96/015868, US Patent No. 6,268, 389. Page numbers in both the WO and US Patent will be provided in the discussion of the contents of the prior art.

The instant claims teach alpha-1-agonist alkylphenyliminoimidazolidine tautomeric equivalent derivatives of formulas I and II (claims 1-10), which are useful in pharmaceutical compositions (claims 11-20) for the treatment of urinary incontinence (claims 21-30). The compounds of formulas I and II can be substituted in the R1, R3 or R5 position by hydrogen, bromine, or chlorine (claims 1-8) and R2 and R4 must have one of the groups being a branched C3-6-alkyl (claim 1) such as tertiary butyl or isopropyl (claims 2-8).

Determining the scope and contents of the prior art

WO 96/32939 discloses phenyliminoimidazolidine tautomeric equivalent derivatives of formulas Ib and II (WO page 2 line 19- page 3 line 22, US column 2 lines 5-50), which are useful in pharmaceutical compositions (WO page 18 line 15-24, US column 11, line 52-64) for the treatment of urinary incontinence (WO page 1 lines 1-3, US column 1 lines 11-13. Preferred compounds of formulas Ib can be substituted at positions R1, R2, R3, and R5 with hydrogen, bromine, chlorine and R4 can be C1-4 alkyl (WO page 4 lines 11- page 5, US column 3 lines 5-33). Alkyl is defined as

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branched or unbranched alkyl groups such as isopropyl and tertiary butyl on page 6 lines 13-18 of WO 96/32939 (US column 4, lines 4-9).

DE 3712385 discloses phenyliminoimidazolidine derivatives of the formula I (page 2, lines 5-10), which are useful in pharmaceutical compositions (page 6) as an alpha1-adrenergic agonist (page 4 line 22). A specific compound disclosed is 2-(2-bromo-6-chloro-4-isopropylphenylimino)-imidazolidine (page 2, line 42).

Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art WO 96/32939 and the claims at issue is that the prior art generically encompasses that which is instantly claimed and discloses preferred embodiments encompassing that which is instantly claimed but does not make a specific compound that falls within the invention as instantly claimed. The difference between the prior art DE 3712385 and the claims at issue is that DE 3712385 discloses a positional isomer of the compounds as instantly claimed.

Resolving the level of ordinary skill in the pertinent art

However, it would have been obvious to someone of ordinary skill in the art at the time of the invention when faced with the prior art to create compounds as instantly claimed wherein R2 or R4 must have one group being a branched C3-C6 alkyl. The motivation to make the claimed compounds derives from the expectation that the instantly claimed compounds would possess similar activity to that which is disclosed in the prior art discussed above. The motivation would come from the disclosure of preferred embodiments of the compound of formula Ib, which is useful for the treatment of urinary incontinence, in WO 96/32939 which prefers R4 being a C1-C4 alkyl and R1, R2, R3, and R5 as hydrogen, bromine, or chlorine and the disclosure of a positional isomer of

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the compounds as instantly claimed in DE 3712385 which are useful for the treatment of urinary incontinence. In regards to DE 3712385, nothing unobvious is seen in substituting the known claimed isomer for the structurally similar isomer, since such structurally related compounds suggest one another and would be expected to share common properties absent a showing of unexpected results. Compare rational in In re Norris, 84 USPQ 458 (1950). Additionally, since applicant is claiming a method of treating urinary incontinence with the compound as instantly claimed, a showing of unobvious and superior properties in using the compounds for this method of treatment would also have to be shown.

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (703) 605-1157. Mrs. Anderson can normally be reached Monday through Friday 7:00AM to 3:30PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph McKane, can be reached at (703) 308-4537.

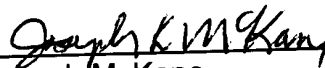
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone numbers are (703) 308-1235 and (703) 308-0196.

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A facsimile center has been established. The hours of operation are Monday through Friday, 8:45AM to 4:45PM. The telecopier numbers for accessing the facsimile machine are (703) 308-4242, (703) 305-3592, and (703) 305-3014.



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